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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/619,148	07/19/00	UCHIDA	K 00631000049

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EXAMINER	
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ART UNIT	PAPER NUMBER
1641	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/619,148	UCHIDA ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2001* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *9-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-12* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicants' response to the Restriction Requirement mailed March 19, 2001 (Paper #7 filed 4/30/01 is acknowledged. In response to the amendment-A filed therein new claim 12 was added while claims 9-11 were amended. Currently, claims 1-12 are pending and under consideration.

Election/Restrictions

2. Applicant request for reconsideration of the Restriction Requirement in light of newly submitted claim (12) and amendments to claims 9-11 was carefully considered but not found persuasive. Although the claims are directed to the detection of LDL and denatured LDL in the preamble, they are still patentable distinct methods having diverse method steps and employing different reagents. Therefore the Restriction is maintained. The following reformulated Restriction Requirement is presented to clarify the present status/grouping of all the pending claims:

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8 are drawn to a method for detecting lower density lipoprotein (LDL) in a blood sample utilizing a measuring complex, classified in class 436, subclass 71, for example.

II. Claims 9-11 are drawn to a method for detecting lower density lipoprotein (LDL) in a blood sample utilizing a measuring complex, an anti-human fibrinogen antibody, a detecting reagent, and a labeled substance classified in class 435, subclass 13, for example.

III. Claim 12 is drawn to a method for detecting lower density lipoprotein (LDL) in a blood sample utilizing a measuring complex along with a high molecular compound or extracellular substrate and a solid phase, classified in class 435, subclass 7.92, for example.

4. The inventions are distinct, each from the other because of the following reasons:

Inventions I, II, and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are directed to three diverse, independent, and distinct methods. Specifically the methods have different modes of operation. Group I only requires the use of a measuring complex, Group II utilizes the measuring complex along with a fibrinogen antibody, while Group III is directed to a method employing a measuring complex, solid phase, and either a high molecular compound or extracellular substrate. These limitations are not totally exclusive to all three methods. Therefore, the three methods utilized different reagents and have different method steps – different modes of operation and are patentably distinct.

It is recognized that although the search for the inventions may overlap they are not totally co-extensive, where the search for one would fully encompass the search for the others. Because these inventions are distinct for the reasons given above and the search required for Inventions of Group I, II and III are not mutually inclusive (i.e. the search for one invention is not required for the other inventions) restriction for examination purposes as indicated is proper.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and **do not** represent all the classes and subclasses which must be searched for each invention; nor is the search limited to issued US patents, but rather includes foreign patents and applications as well as literature searches.

6. The Restriction Requirement is still deemed proper for reasons set forth above and is therefore made **FINAL.**

7. Currently claims 9-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made with traverse in Paper No.7. Claims 1-8 are pending and currently under consideration.

Oath/Declaration

8. A new oath or declaration is required because it does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. See MPEP §§ 602.01 and 602.02.

Priority

9. Receipt is acknowledged of papers submitted (Paper34, filed 9/28/00) under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

10. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). This application does not contain the required first sentence of the specification referencing foreign application No. 11-207913 filed 7/22/99 in Japan and foreign application No. 2000-12210 filed 1/20/00 in Japan. Please add to the specification.

11. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Drawings

12. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the examiner allows the application.

Information Disclosure Statement

13. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 has cited the references they have not been considered.

Specification

14. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and confusing. The preamble of the claim recites "detecting LDL and denatured LDL". Is this meant to say that the method is detecting "normal", not denatured LDL, or both LDL and denatured LDL? However, the body of the claim is directed to measuring either LDL or denatured LDL.

B. In claim 1 is vague and indefinite because it is not clear how the claimed method will distinguish between LDL and denatured LDL. The method appears to simply utilizes a complex of either LDL or denatured LDL that is not oxidatively denatured, but does not give any indication of complex formation, complex detection, or a correlation step relating the measured complex to the analysis of LDL and denatured LDL.

C. Claim 1, line 5 recites "LDL is not oxidatively denatured". This is vague because it is not known if applicant is referring to the lower density lipoprotein or denatured lower density lipoprotein. Both are previously cited. Please clarify.

D. The use of parentheses, (i.e. in claim 1, line 5) is indefinite because it is parenthetical and does not provide positive limitations to the claim. It is suggested that Applicant remove the parentheses to obviate the rejection.

E. Regarding claims 2-8, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

F. Regarding claims 2-8, the phrase "and/or the like" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "or the like"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

G. Claims 2-8 are in improper "markush form". As recited it is not clear as to what the measuring complex will contain. Therefore the claims are vague and indefinite. Is it Applicants intent to claim a measuring subject complex containing, either an acute phase reactant, coagulation-fibrinolytic related protein, or a disinfectant substance produced by a macrophage that further contains LDL or denatured LDL? Or is it Applicants intent to claim a measuring subject complex containing, either an acute phase reactant, coagulation-fibrinolytic related protein, or a disinfectant substance produced by a macrophage wherein LDL or denatured LDL are not apart of the initial complex but introduced via the blood sample to be tested?

Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See Ex parte Markush, 1925 C.D. 126 (Comm'r Pat. 1925). It is suggested that applicant utilize proper Markush form to clarify the claims and obviate this rejection.

H. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below:

The claims particularly, independent claim 1 is drawn to an assay method that employs a measuring subject complex. But the claim merely recites the detection of LDL and denatured LDL using this complex, such claim language is not sufficient to support the method claim. An assay or method, as proposed in the preamble of claim 1 require at least a contact step between reagents and sample, the separation of unbound and bound material, a detection step, and a correlation step. These essential steps for the method have not been outlined for LDL and denatured LDL. It is suggested that Applicant add steps that at least reflect: (I) a sample and reagent contacting step, (II) the binding or complex formation of a detectable product, and (III) a correlation step. Please add appropriate steps.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Boullier et al. (Clinica Chimica Acta, 238, pages 1-10, 1995).

Boullier et al. teach an enzyme-linked immunosorbent assay to detect oxidized low-density lipoprotein immune complexes in blood samples. See abstract and page 2. Specifically malondialdehyde (MDA) the predominant epitope of ox LDL in atherosclerotic lesions was prepared as the antigen. Page 3, Section 2.3. The method distinguished between native LDL and oxLDL via the monoclonal antibody BL3. Page 5, Section 2.6.

II. Claims 1 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Koren et al. (WO 96/000903).

Koren et al. teach immunological measuring methods employing monoclonal antibodies to determine apolipoproteins and lipoproteins, including Apo B-100, Apo A-I, Apo A-II, Apo C-III, and Apo E and thereby detecting relative ratios of HDL, LDL, LpaI, and LpaII. The method is operable in human blood, serum, or plasma. In one embodiment the reagents are bound to a solid phase (dipstick) which is exposed to the sample to be tested. See abstract and page 14.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 2-4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boullier et al. (Clinica Chimica Acta, 238, pages 1-10, 1995) and Koren et al. (WO 96/000903). in view of Kaiserling et al. (Gastroenterology, 1996, Vol.110, pages 369-374) and .

Please see previous discussions of Boullier et al. and Koren et al. as set forth above.

Boullier et al. and Koren et al. differ from the instant invention in failing to teach the specific detection of measuring complexes involving particular acute phase reactants, blood coagulation-fibrinolytic related proteins, or disinfectant substances produced by macrophages in blood cells.

However, Kaiserling et al. taught several measuring subject complexes that could be utilized in analyzing the morphology and immunophenotype of cells expressing low density lipoprotein (LDL) and oxidized LDL. See page 369, 2nd column, 4th paragraph. Numerous antibody compositions were used as possible mechanisms to determine LDL and ox-LDL in lipid cells. These antibodies include limitations found in claims 2-4, i.e alpha 1 –antitrypsin. See Table 1. Lysozyme reactivity is also discussed. See page 371, Immunohistochemical Findings.

Boullier et al., Koren et al., and Kaiserling et al. are all analogous art because they are from the same field of endeavor, all three inventions teach LDL and ox-LDL measurement techniques.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use various measuring subject complexes as taught by Kaiserling et al. in either method of Boullier et al. or Koren et al. to detect LDL and ox-LDL, because such measuring subject complexes as taught by Kaiserling et al. are well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing various measuring subject complexes because Kaiserling et al. taught that during the process of modification LDL loses its ability to bind classical LDL receptors. The modified types of LDL (oxidized and acetylated) bind one or more classes of scavenger receptors (multifunctional lipoprotein-binding receptors). See page 373, 2nd column, 3rd paragraph.

One having ordinary skill in the art would have been motivated to do this because the prior art does not contain information on all the possible complexes involving LDL and ox-LDL. Kaiserling et al. page 373, 1st paragraph, 3-4 lines. Therefore the detection of multiple complexes would render more data sets for further consideration and possible functional analysis.

With respect to the various measuring complexes outlined in the claims, these particular measuring complexes all include known compositions which are viewed as routine optimizations that are almost always determined and used in immunoassay studies.

Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to substitute known measuring complexes in the given parameters to determine the unknown as a means of optimizing the assays provided by the art.

Remarks

18. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Koren et al. (U.S. Patent#6,107,045) disclose monoclonal antibodies and methods to determine the concentration of lipoproteins in blood, serum, or plasma samples.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO fax center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 35-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
Patent Examiner
Art Unit 1641
CM1-7B17

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641